CLINICAL RESEARCH STUDIES

From the Society for Vascular Surgery

Differential outcomes of carotid stenting and endarterectomy performed exclusively by vascular surgeons in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST)

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Objective: **Outcomes in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) did not differ between carotid artery stenting (CAS) and carotid endarterectomy (CEA) for the composite primary end point of stroke, myocardial infarction (MI), or death during the periprocedural period or ipsilateral stroke within 4 years. Rigorous credentialing and training of interventionists, including vascular surgeons, were required for the randomization phase of CREST. Because the lead-in phase of CREST had suggested higher perioperative risks after CAS performed by vascular surgeons, the purpose of this analysis was to examine differences in outcomes after randomization between CAS and CEA performed by vascular surgeons.**
Methods: **CREST is a prospective randomized controlled trial with blinded end point adjudication. Vascular surgeons performed 237 (21%) of the CAS procedures and 765 (65%) of the CEA procedures among 2320 patients who received their assigned treatment. Proportional hazards analyses were used to estimate the relative efficacy of CAS vs CEA for the composite primary end point and also for stroke and death.**
Results: **Among 2502 randomized patients, 1321 (53%) were symptomatic and 1181 (47%) were asymptomatic. For procedures performed exclusively by vascular surgeons, the primary end point did not differ between CAS and CEA at 4-year follow-up (6.2% vs 5.6%, respectively; hazard ratio [HR], 1.30; 95% confidence interval [CI], 0.70-2.41; $P = .41$) In this subgroup, the periprocedural stroke and death rates were higher after CAS than CEA for symptomatic patients (6.1% vs 1.3%; $P = .01$). Asymptomatic patients also had slightly higher stroke and death rates after CAS (2.6% vs 1.1%; $P = .20$), although this difference did not reach statistical significance. Conversely, cranial nerve injuries (0.0% vs 5.0%; $P < .001$) were less frequent after CAS than CEA. The MI rates were slightly lower after CAS (1.3% vs 2.6%; $P = .24$). In performing CAS, vascular surgeons had outcomes for the periprocedural primary end point comparable to the outcomes of all interventionists (HR, 0.99; 95% CI, 0.50-2.00) after adjusting for age, sex, and symptomatic status. Vascular surgeons also had similar results after CEA for the periprocedural primary end point compared with other surgeons (HR, 0.73; 95% CI, 0.42-1.27).**
Conclusions: **When performed by surgeons, CAS and CEA have similar net outcomes, although the periprocedural risks vary (lower stroke with CEA and lower MI with CAS). These data suggest that appropriately trained vascular surgeons may safely offer both CEA and CAS for the prevention of stroke. The remarkably low stroke and death rates after CEA performed by vascular surgeons in CREST, particularly among symptomatic patients, represent the best outcomes ever reported after carotid interventions from a randomized controlled trial. ClinicalTrials.gov identifier: NCT0000473. (J Vasc Surg 2013;57:303-8.)**

Both carotid endarterectomy (CEA) and carotid artery stenting (CAS) are effective interventions in preventing stroke and death among patients with significant carotid stenosis.[1-7] Although CAS initially was reserved for patients with a high surgical risk for CEA,[8,9] recent clinical trials have revealed that CAS may also be an alternative for conventional risk

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patients.[6,10] In fact, comparison of standard risk patients in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) did not reveal any significant differences between CAS and CEA for the primary end point.[6,11] Periprocedural stroke, myocardial infarction (MI), or death and ipsilateral stroke up to 4 years were similarly low for both CAS and CEA, although a higher risk of stroke with CAS and a higher risk of MI with CEA were observed. A planned meta-analysis of European trials also failed to detect treatment differences among symptomatic patients younger than 70 years.[10]

Certification of surgeons and interventionists who performed CAS and CEA in CREST was required prior to randomizing patients.[6,12] Although some interventionists were certified after satisfactory evaluation of their endovascular experience and CAS results, most underwent rigorous hands-on training and auditing of their outcomes by participation in the lead-in phase. Interestingly, the results of the lead-in phase of CREST suggested higher perioperative risks after CAS performed by vascular surgeons.[12] Stroke, death, and MI rates at 30 days by specialty in the lead-in phase were 7.7% for vascular surgery, 6.7% for neurosurgery, 1.6% for neuroradiology, 6.6% for interventional radiology, and 3.9% for interventional cardiology. After adjustment for age, vascular surgeons had a twofold higher event rate than interventional cardiologists (odds ratio, 2.05; 95% confidence interval [CI], 1.18-3.56). Event rates did not differ significantly among other specialists.

The purpose of this study was to examine differences in outcomes between CAS and CEA performed by vascular surgeons in CREST. Specifically, data from the periprocedural period and up to 4 years were used to contrast the results of CEA and CAS performed by vascular surgeons and other specialists. Furthermore, the relative efficacy of the certification and training process for all interventionists was assessed.

METHODS

Details of the trial design and primary results of CREST have been reported.[6,11] CREST is a multicenter randomized clinical trial with blinded end point adjudication that compared the safety and efficacy of CAS vs CEA in patients with carotid stenosis. Patients were enrolled at 117 clinical centers in the United States and Canada. Ethics review boards at participating centers approved the protocol and informed consent, and all patients gave written informed consent. To be eligible for the study, symptomatic patients required ≥50% ipsilateral carotid stenosis by angiography, ≥70% by duplex ultrasound scanning, or ≥70% by computed tomographic angiography or magnetic resonance angiography if the stenosis on ultrasound scan was 50% to 69%, whereas asymptomatic patients needed ≥60% stenosis by angiography, ≥70% by ultrasound scanning, or ≥80% by computed tomographic angiography or magnetic resonance angiography if the stenosis on ultrasound scan was 50% to 69%. Full eligibility criteria have been reported.[6,11]

Patients randomized to CAS were treated with aspirin and clopidogrel 48 hours before and for 30 days after the procedure. The ACCUNET and ACCULINK carotid stenting systems by Abbott Vascular Solutions, Inc (formerly Guidant; Santa Clara, Calif) were used for CAS procedures. Patients who underwent CEA received aspirin at least 48 hours before and for 1 year or more after the procedure. Full details of the procedures were reported elsewhere.[13]

Participating surgeons and interventionists were carefully selected by a well-documented process.[12,14] Certification was achieved by 477 surgeons, who documented that they had performed more than 12 procedures per year and that the rates of complications and death were <3% among asymptomatic patients and <5% among symptomatic patients. The 224 certified interventionists had to demonstrate experience in CAS with optimal results, receive hands-on experience with the RX ACCULINK stent and the RX ACCUNET embolic protection device, or participate in a lead-in phase prior to randomizing patients. Most interventionists participated in the training program and the lead-in phase. Only 73 of the initial 427 potential applicants (17%) had clinical registry experience and satisfactory results with the devices used in CREST and therefore were exempt from training and were approved for the randomization phase.

Periprocedural neurologic evaluations were conducted preprocedurally, at 24 to 48 hours postprocedurally, and at 1 month, 3 months, and annually. Cardiac enzyme levels were obtained preprocedurally, at 24 to 48 hours postprocedurally, and for chest pain lasting >15 minutes. Electrocardiograms were completed preprocedurally, 24 to 48 hours postprocedurally, and for chest pain lasting >15 minutes. Myocardial infarction was defined as biomarker elevation plus either chest pain or electrocardiographic evidence of ischemia.

For the purpose of this study, similar statistical analyses to those for the CREST primary results were used.[6] On-treatment end point analyses adjusting for major baseline covariates were conducted using standard time-to-event statistical modeling. In addition to the primary end point, outcome differences among specialists were assessed for components of the composite end point and periprocedural risk. Because this analysis was performed for a subgroup of patients and only for those receiving therapy, the comparison of CEA with CAS is not protected by randomization. As such, differences between treatment efficacy for patients treated by CAS or CEA could be due to the differential skills of the vascular surgeons for the two procedures or alternatively due to differences in the type of patients receiving CAS/CEA treatment. In order to remove the potential effect of the latter source of differences, proportional hazards analysis was done, adjusting for age, sex, and symptomatic status, the primary factors shown to be associated with outcomes. Secondary aims were analyzed by including interaction terms in the proportional hazards models. For complication rates, the periprocedural period was defined according to the study protocol as the 30-day period after the procedure. The absolute differences in event proportions were calculated as the percentage of patients with events.

RESULTS

Between December 21, 2000, and October 16, 2008, 176 vascular surgeons performed 1002 (43%) of the carotid interventions among the 2320 patients who received their assigned treatment in the randomization phase. Of these interventions, vascular surgeons performed 237 of the 1136 CAS procedures (21%) and 765 of the 1184 CEAs (65%). Among randomized patients who underwent carotid interventions by vascular surgeons, 467 (46.6%) were symptomatic and 535 (53.4%) were asymptomatic. As with the entire CREST cohort, there were no significant differences in baseline characteristics between the CAS and CEA patient groups, except for the percent asymptomatic CAS patients compared with CEA patients (65.4% vs 49.7%) and previous history of coronary artery disease or coronary artery bypass graft surgery (39.3% vs 47.5%; Table I). Among procedures performed by vascular surgeons, embolic protection was used in 229 (98.7%) of the CAS procedures, whereas for CEA general anesthesia and a patch were used in 647 (84.8%) and 616 (80.7%), respectively.

Primary end point rates were not significantly different between CAS and CEA for procedures performed exclusively by vascular surgeons at 4-year follow-up (6.2% vs 5.6%, respectively; hazard ratio [HR], 1.30; 95% CI, 0.70-2.41; $P = .41$; Table II). These primary end point rates were slightly lower than originally reported for CAS vs CEA for the entire CREST cohort (7.2% vs 6.8%; HR, 1.11; 95% CI, 0.81-1.51; $P = .51$). Similarly, the periprocedural primary end point rates did not differ for CAS and CEA (4.2% vs 3.8%, respectively; HR, 1.26; 95% CI, 0.61-2.60; $P = .54$). After the periprocedural period, the incidence of ipsilateral stroke was similarly low after CAS and CEA performed by vascular surgeons (2.1% and 1.8%, respectively; $P = .63$).

Among randomized patients who underwent the assigned intervention performed by vascular surgeons, the periprocedural stroke and death rates were higher after CAS than CEA among symptomatic patients (6.1% vs 1.3%; HR, 4.84; 95% CI, 1.40-16.74; $P = .01$) and among asymptomatic patients (2.6% vs 1.1%; HR, 2.50; 95% CI, 0.63-9.99; $P = .20$). Conversely, MI rates were lower for CAS compared with CEA (1.3% vs 2.6%; $P = .24$). As expected, cranial nerve injuries (0.0% vs 5.0%) were less frequent after CAS than CEA. Levels of significance merit conservative interpretation because of differences in number of events (10 periprocedural stroke and death events for symptomatic patients, eight stroke and death events for asymptomatic patients, 12 MI events for symptomatic patients, and 11 MI events in asymptomatic patients).

When vascular surgeons were compared with all other specialists performing CAS, they had comparable outcomes for the periprocedural primary end point (HR, 0.99; 95% CI, 0.50-2.00) after adjusting for age, sex, and symptomatic status (Table III). Vascular surgeons also had similar results after CEA for the periprocedural primary end point compared with other specialists performing CEA (HR, 0.73; 95% CI, 0.42-1.27).

Table I. Baseline characteristics of the study population according to treatment group

Characteristic	*CAS (N = 237)*	*CEA (N = 765)*	P *value*
Age, mean (SD), years	68.5 (8.0)	69.4 (8.6)	.13
Median	68.5	70.3	—
Interquartile range	11.1	12.7	—
Male gender, %	68.8	67.1	.62
White race, %	89.9	92.6	.19
Asymptomatic arteries, %	65.4	49.7	<.001
Risk factor, %			
Hypertension	82.6	85.2	.33
Diabetes	26.7	29.5	.40
Dyslipidemia	79.2	84.0	.09
Current tobacco smoking	28.5	25.9	.43
Treatment with cholesterol medications	93.0	90.0	.22
Coronary artery disease or coronary artery bypass graft surgery	39.3	47.5	.03
Percent stenosis at randomization			
Severe (≥70%)	91.6	87.2	.07
Anatomic characteristic			
Left carotid artery treated	46.8	52.7	.12
Contralateral occlusion	—	—	—
Procedural characteristic			
Target lesion length, mean (SD), mm	19.5 (8.8)	—	—
Median	19.5	—	—
Interquartile range	12.0	—	—
Total length of stented segment, mean (SD), mm	34.7 (8.2)	—	—
Balloon angioplasty before stenting, %	73.4	—	—
Embolic protection, %			
Was patient eligible for embolic protection device?	99.6	—	—
Was it successfully delivered?	98.7	—	—
General anesthesia, %	—	84.8	—
Surgical technique, %			
Patch	—	80.7	—
Shunt	—	59.1	—

CAS, Carotid artery stenting; *CEA,* carotid endarterectomy; *SD,* standard deviation.
Sample sizes vary for specific characteristics (rows) because of missing data on specific items for a small number of patients.

DISCUSSION

The results of this substudy of CREST, the largest randomized clinical trial comparing carotid interventions for stroke prevention among conventional risk patients, failed to detect differences in the primary end point of periprocedural stroke, death, and MI and ipsilateral stroke thereafter between CAS and CEA performed by appropriately trained vascular surgeons. As in the entire CREST cohort, the periprocedural risks vary (lower stroke with CEA and lower MI with CAS), which is predominantly seen among patients with symptomatic carotid stenosis.[6] Of note, the periprocedural stroke and death rates after CEA performed by vascular surgeons for symptomatic

Table II. Treatment effect on time to first primary end point, components of the primary end point, and other events for vascular surgeons (n = 1002)

	Periprocedural period				*Four-year period*			
	CAS, no. of events (rate ± SE)	*CEA, no. of events (rate ± SE)*	*HR (95% CI)*	P *value*	*CAS, no. of events (rate ± SE)*	*CEA, no. of events (rate ± SE)*	*HR (95% CI)*	P *value*
MI end point								
Overall	3 (1.3 ± 0.7)	20 (2.6 ± 0.6)	0.48[a] (0.14-1.62)	.24				
Symptomatic	2 (2.4 ± 1.7)	10 (2.6 ± 0.8)	0.93[a] (0.20-4.25)	.93				
Asymptomatic	1 (0.6 ± 0.6)	10 (2.6 ± 0.8)	0.25[a] (0.03-1.91)	.18				
Stroke and death end point (any stroke or death within periprocedural period and postprocedural ipsilateral stroke)								
Overall	9 (3.8 ± 1.2)	9 (1.2 ± 0.4)	3.94 (1.53-10.10)	.004	14 (6.2 ± 1.6)	20 (3.1 ± 0.7)	2.76 (1.37-5.55)	.004
Symptomatic	5 (6.1 ± 2.6)	5 (1.3 ± 0.6)	4.84[a] (1.40-16.74)	.013	6 (7.4 ± 2.9)	13 (3.8 ± 1.1)	2.45 (0.92-6.48)	.07
Asymptomatic	4 (2.6 ± 1.3)	4 (1.1 ± 0.5)	2.50[a] (0.63-9.99)	.20	8 (5.6 ± 2.0)	7 (2.4 ± 1.0)	3.10 (1.12-8.59)	.03
Primary end point (any stroke, MI, or death within periprocedural period and postprocedural ipsilateral stroke)								
Overall	10 (4.2 ± 1.3)	29 (3.8 ± 0.7)	1.26 (0.61-2.60)	.54	14 (6.2 ± 1.6)	39 (5.6 ± 0.9)	1.30 (0.70-2.41)	.41
Symptomatic	6 (7.3 ± 2.9)	15 (3.9 ± 1.0)	2.01 (0.78-5.20)	.15	6 (7.3 ± 2.9)	22 (6.1 + 1.3)	1.36 (0.55-3.38)	.50
Asymptomatic	4 (2.6 ± 1.3)	14 (3.7 ± 1.0)	0.75 (0.24-2.29)	.62	8 (5.6 ± 2.0)	17 (5.1 ± 1.3)	1.25 (0.54-2.89)	.61

CAS, Carotid artery stenting; *CEA,* carotid endarterectomy; *CI,* confidence interval; *HR,* hazard ratio; *MI,* myocardial infarction; *SE,* standard error.
[a]Univariate proportional hazards model used because of the small number of events.

Table III. Periprocedural end points by treatment group for vascular surgeons compared with all other specialists

	CAS procedures				*CEA procedures*			
Periprocedural events	*Vascular surgeons*	*Other specialists*	*HR (95% CI)*	P *value*	*Vascular surgeons*	*Other specialists*	*HR (95% CI)*	P *value*
Stroke and death end point (any stroke or death within periprocedural period)								
Overall	9 (3.8 ± 1.2)	40 (4.5 ± 0.7)	1.12 (0.54-2.35)	.76	9 (1.2 ± 0.4)	16 (3.8 ± 0.9)	0.32 (0.14-0.72)	.006
Symptomatic	5 (6.1 ± 2.6)	31 (6.1 ± 1.1)	1.11 (0.43-2.86)	.83	5 (1.3 ± 0.6)	12 (5.0 ± 1.4)	0.27[a] (0.09-0.76)	.013
Asymptomatic	4 (2.6 ± 1.3)	9 (2.4 ± 0.8)	1.09[a] (0.33-3.52)	.89	4 (1.1 ± 0.5)	4 (2.2 ± 1.1)	0.47[a] (0.12-1.87)	.28
Primary end point (any stroke, MI, or death within periprocedural)								
Overall	10 (4.2 ± 1.3)	48 (5.4 ± 0.8)	0.99 (0.50-2.0)	.99	29 (3.8 ± 0.7)	22 (5.3 ± 1.1)	0.73 (0.42-1.27)	.26
Symptomatic	6 (7.3 ± 2.9)	35 (6.9 ± 1.1)	1.19 (0.50-2.84)	.70	15 (3.9 ± 1.0)	16 (6.7 ± 1.6)	0.59 (0.29-1.19)	.14
Asymptomatic	4 (2.6 ± 1.3)	13 (3.5 ± 0.9)	0.74 (0.24-2.26)	.59	14 (3.7 ± 1.0)	6 (3.4 ± 1.3)	1.09 (0.42-2.84)	.86

CAS, Carotid artery stenting; *CEA,* carotid endarterectomy; *CI,* confidence interval; *HR,* hazard ratio; *MI,* myocardial infarction.
[a]Univariate proportional hazards model employed because of the small number of events.

carotid stenosis are the lowest ever reported for any carotid intervention among symptomatic patients.

The periprocedural stroke and death rates for CAS and CEA performed by vascular surgeons in CREST are the lowest ever reported not only for interventions for symptomatic carotid stenosis but also for asymptomatic carotid disease (Figs 1 and 2). Moreover, both stroke and death rates are well below the targets of 6% for symptomatic patients and 3% for asymptomatic patients suggested in recent treatment guideline statements.[4,5,15]

As reported in this study and the original CREST publication, both CAS and CEA can be performed with optimal periprocedural outcomes by experienced surgeons and interventionists, including vascular surgeons.[6] In many instances, vascular surgeons potentially could offer both procedures. Of note, CREST vascular surgeons were able to perform CEA with a significantly lower periprocedural risk of stroke and death compared with surgeons and other interventionists performing CAS. A higher MI rate with CEA and the added risk of postoperative cranial nerve palsies are still matters of concern. Fortunately, cranial nerve palsies and MI did not have the same impact on physical and mental health as stroke based on quality-of-life assessment.[6,16] The higher rate of periprocedural stroke after CAS has fallen over time, as has the periprocedural risk of stroke after CEA. The periprocedural risk of CAS

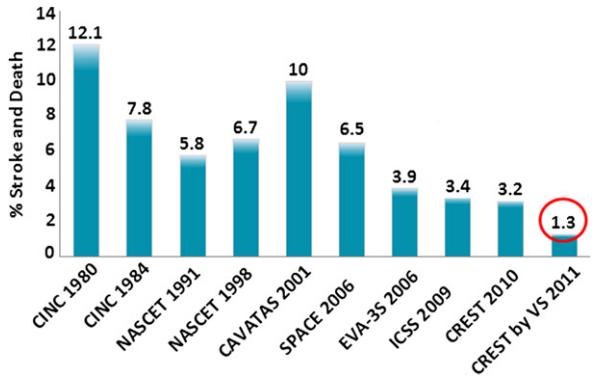

Fig 1. Perioperative stroke and death rate for carotid endarterectomy in symptomatic patients. *CAVATAS,* Carotid and Vertebral Artery Transluminal Angioplasty Study[17]; *CINC 1980,* Cincinnati 1980[18]; *CINC 1984,* Cincinnati 1984[18]; *CREST,* Carotid Revascularization Endarterectomy versus Stenting Trial[6]; *CREST by VS,* CREST by vascular surgeons; *EVA-3S,* Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis trial[19]; *ICSS,* International Carotid Stenting Study[20]; *NASCET 1991,* North American Symptomatic Carotid Endarterectomy Trial[21]; *NASCET 1998,* North American Symptomatic Carotid Endarterectomy Trial 1998[22]; *SPACE,* Stent-protected Angioplasty versus Carotid Endarterectomy trial.[23]

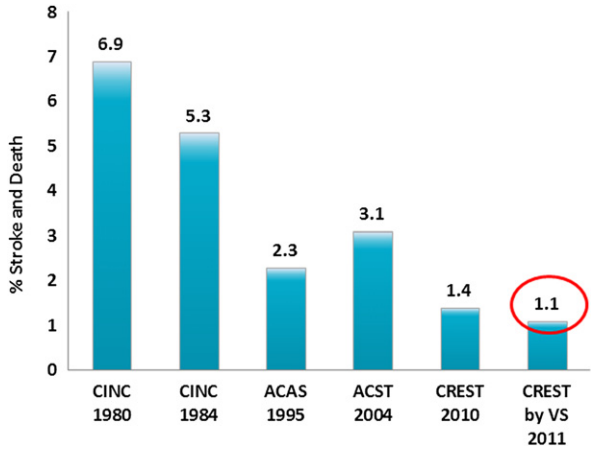

Fig 2. Perioperative stroke and death rate for carotid endarterectomy in asymptomatic patients. *ACAS,* Asymptomatic Carotid Atherosclerosis Study[3]; *ACST,* Asymptomatic Carotid Surgery Trial[24]; *CINC 1980,* Cincinnati 1980[18]; *CINC 1984,* Cincinnati 1984[18]; *CREST,* Carotid Revascularization Endarterectomy versus Stenting Trial[6]; *CREST by VS,* CREST by vascular surgeons.

in our study appears to be comparable between vascular surgeons and interventionists from other specialties.

Interventionists' training, experience, and specialty have been suggested as important factors for optimal outcomes after CAS procedures.[12] In the CREST lead-in phase, higher periprocedural event rates were seen for procedures performed by vascular surgeons and marginally higher rates for interventional radiologists compared with cardiologists.[12] These differences were attributed primarily to experience with catheter-based therapies and particularly CAS, and possibly to the complexity of the cases referred to specific specialties rather than to the specialty itself.

Multivariate analyses of lead-in phase data were performed in an attempt to adjust for potential confounders, including symptomatic status, degree of stenosis, and age. In these multivariate models, only age and interventionist specialty remained significant predictors of major adverse events after CAS. After adjustment for age, vascular surgeons had a higher event rate than did interventional cardiologists, whereas event rates did not differ significantly among interventional radiologists, neurosurgeons, and interventional neuroradiologists. For the randomization phase, only interventionists with a proven track record and optimal results in CAS techniques, irrespective of their specialty, were allowed to perform carotid stenting.[6]

The reduced stroke and death rates in CREST, particularly for procedures performed by vascular surgeons, as compared with previous trials and other specialists, may reflect the effective surgeon credentialing in CEA, assimilation of advanced endovascular technology, and rigorous training and credentialing of interventionists performing CAS. Although the certification requirements were important for patient safety, they limit the generalizability of the results and conclusions to similarly qualified operators, which constitutes one of the main limitations of CREST. Of the 427 stent operators who applied for the trial, only half (224 [52.4%]) ultimately were approved for the randomization phase.[12] The effects of experience in performing carotid interventions or the number of cases performed before the randomization on 30-day outcomes could not be defined with the available data and is beyond the scope of this substudy. Total catheter experience, total endovascular treatment experience, or total carotid treatment experiences were not directly and objectively assessed during the trial. The more experienced interventionists were required to perform fewer cases in the lead-in phase than the less experienced ones, making the benefits of experience more difficult to detect from the lead-in phase results. The potential influence of patient and operator characteristics on the outcomes in CREST and other randomized carotid intervention trials remains unknown and warrants further investigation.

The stroke and death rates after CAS performed by vascular surgeons were acceptable and within the targets suggested by the American Heart Association/American Stroke Association guidelines for the outcomes of carotid interventions.[7] However, the outcomes after CEA performed by vascular surgeons were superior in terms of periprocedural stroke and death rates: 1.3% for symptomatic patients and 1.1% for asymptomatic patients. These improved outcomes after CEA in CREST may have several implications. First, the remarkably low stroke and death rates after CEA performed by vascular surgeons call for a revision of the accepted periprocedural outcomes and guidelines for carotid interventions. We suggest that the guideline rates for periprocedural stroke and death of <6% for symptomatic patients and <3% for asymptomatic

patients are too high. Second, vascular surgeons with current training and experience in both CAS and CEA are well positioned to take care of patients with carotid disease because they may be able to choose from among the different options of treatment impartially and without bias. Third, the improved outcomes with CEA in terms of stroke and death call for improved outcomes with CAS. Better outcomes following CAS may require improved systems for embolic protection and stent design.

CONCLUSIONS

When performed by appropriately trained vascular surgeons, CAS and CEA have similar net outcomes, although the periprocedural risks vary (lower stroke with CEA and lower MI with CAS). Trained vascular surgeons may safely offer both CEA and CAS for the prevention of stroke. As for all interventionists/operators, focus on preventing periprocedural events is of high priority for vascular surgeons. The remarkably low stroke and death rates after CEA performed by vascular surgeons in CREST represent the best outcomes ever reported after carotid interventions from a randomized controlled trial.

AUTHOR CONTRIBUTIONS

Conception and design: CT, VM, MM, OB, BL, WM, JV, TB
Analysis and interpretation: CT, JV, TB
Data collection: JV, TB
Writing the article: CT, VM, MM, OB, BL, WM, JV, TB
Critical revision of the article: CT, VM, MM, OB, BL, WM, JV, TB
Final approval of the article: CT, VM, MM, OB, BL, WM, JV, TB
Statistical analysis: CT, JV
Obtained funding: TB
Overall responsibility: CT

REFERENCES

1. Wolf PA, Kannel WB, Gee DL. Epidemiology of strokes in North America. In: Barnett HJM, Stein BM, Mohr JP, Yatsu FM, editors. Stroke: Pathophysiology, diagnosis and management. New York: Churchill Livingstone; 1986. p. 19-29.
2. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med 1991;325:445-53.
3. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. JAMA 1995;273:1421-8.
4. Moore WS, Barnett HJ, Beebe HG, Bernstein EF, Brener BJ, Brott TG, et al. Guidelines for carotid endarterectomy. A multidisciplinary consensus statement from the Ad Hoc Committee, American Heart Association. Circulation 1995;91:566-79.
5. Biller J, Feinberg WM, Castaldo JE, Whittemore AD, Harbaugh RE, Dempsey RJ, et al. Guidelines for carotid endarterectomy: a statement for healthcare professionals from a Special Writing Group of the Stroke Council, American Heart Association. Circulation 1998;97:501-9.
6. Brott TG, Hobson RW 2nd, Howard G, Roubin GS, Clark WM, Brooks W, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med 2010;363:11-23.
7. Furie KL, Kasner SE, Adams RJ, Albers GW, Bush RL, Fagan SC, et al. Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2011;42:227-76.
8. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med 2004;351:1493-501.
9. Fairman R, Gray WA, Scicli AP, Wilburn O, Verta P, Atkinson R, et al. The CAPTURE registry: analysis of strokes resulting from carotid artery stenting in the post approval setting: Timing, location, severity, and type. Ann Surg 2007;246:551-6.
10. Bonati LH, Dobson J, Algra A, Branchereau A, Chatellier G, Fraedrich G, et al. Short-term outcome after stenting versus endarterectomy for symptomatic carotid stenosis: a preplanned meta-analysis of individual patient data. Lancet 2010;376:1062-73.
11. Sheffet AJ, Roubin G, Howard G, Howard V, Moore W, Meschia JF, et al. Design of the Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST). Int J Stroke 2010;5:40-6.
12. Hopkins LN, Roubin GS, Chakhtoura EY, Gray WA, Ferguson RD, Katzen BT, et al. The Carotid Revascularization Endarterectomy versus Stenting Trial: credentialing of interventionalists and final results of lead-in phase. J Stroke Cerebrovasc Dis 2010;19:153-62.
13. Silver FL, Mackey A, Clark WM, Brooks W, Timaran CH, Chiu D, et al. Safety of stenting and endarterectomy by symptomatic status in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST). Stroke 2011;42:675-80.
14. Hobson RW II, Howard VJ, Roubin GS, Ferguson RD, Brott TG, Howard G, et al. Credentialing of surgeons as interventionalists for carotid artery stenting: experience from the lead-in phase of CREST. J Vasc Surg 2004;40:952-7.
15. Ricotta JJ, Aburahma A, Ascher E, Eskandari M, Faries P, Lal BK. Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease. J Vasc Surg 2011;54:e1-31.
16. CREST trial. Supplementary Appendix. Available at: http://www.nejm.org/doi/suppl/10.1056/NEJMoa0912321/suppl_file/nejmoa0912321_appendix.pdf. Accessed December 27, 2010.
17. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. Lancet 2001;357:1729-37.
18. Brott TG, Labutta RJ, Kempczinski RF. Changing patterns in the practice of carotid endarterectomy in a large metropolitan area. JAMA 1986;255:2609-12.
19. Mas JL, Chatellier G, Beyssen B, Branchereau A, Moulin T, Becquemin JP, et al. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. N Eng J Med 2006;355:1660-71.
20. Ederle J, Dobson J, Featherstone RL, Bonati LH, van der Worp HB, de Borst GJ, et al. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomised controlled trial. Lancet 2010;375:985-97.
21. The North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 1991;325:445-53.
22. Barnett HJ, Taylor DW, Eliasziw M, Fox AJ, Ferguson GG, Haynes RB, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Eng J Med 1998;339:1415-25.
23. Ringleb PA, Allenberg J, Bruckmann H, Eckstein HH, Fraedrich G, Hartmann M, et al. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial. Lancet 2006;368:1239-47.
24. Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, et al. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. Lancet 2004;363:1491-502.

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